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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/605,577	06/28/2000	Wei Wang	MSB-7267	5817

7590 07/30/2002

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EXAMINER  
SEHARASEYON, JEGATHEESAN

ART UNIT	PAPER NUMBER
1647	12

DATE MAILED: 07/30/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

FILED

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/605,577	WANG ET AL.	
	Examiner Jegatheesan Seharaseyon	Art Unit 1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) Responsive to communication(s) filed on 10 December 2001.
- 2a) This action is FINAL.      2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) Claim(s) 1-6,9 and 10 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 1-6,9 and 10 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) Notice of References Cited (PTO-892)      4) Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_.  
 2) Notice of Draftsperson's Patent Drawing Review (PTO-948)      5) Notice of Informal Patent Application (PTO-152)  
 3) Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_.      6) Other:

## **DETAILED ACTION**

1. The request to reconsider faxed on 12/10/01 (Paper No: 11) is acknowledged. The office is withdrawing the final office action mailed on 10/24/01 in order to reconsider the rejections and apply new art.
2. The text of those sections of Title 35, U. S. Code not included in this action can be found in a prior Office action.

### ***Claim Rejections - 35 USC § 102***

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Patel et al. (U.S. Patent No: 5,358, 708).

The instant invention is directed a pharmaceutical composition comprising human IL-2 or a variant stabilized with histidine.

Patel et al. teaches the stabilization of pharmaceutical formulation of interferon with histidine (abstract). The histidine is present at concentration of 2mg/ml (column 4, lines 35-45). Therefore, the disclosure of Patel et al. anticipates claim 1.

### ***Claim Rejections - 35 USC § 103***

4. Claims 1-3, 5 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over

Patel et al. (U.S. Patent No: 5,358, 708) in view of Hora et al. (U.S. Patent No. 5,078,997)

The instant invention is directed a pharmaceutical composition comprising human IL-2 or a variant stabilized with amino acids, sucrose and salt.

The relevance of Patel et al. has been set forth above in paragraph 3. However, Patel et al. does not explicitly recite a pharmaceutical composition comprising human IL-2 or a variant stabilized with amino acids, sucrose and salt.

Hora et al. discloses the stabilization of IL-2 with sugars, amino acids, vitamins, fatty acids, polymers or low molecular weight acids (column 6, lines 11-60). The reference teaches that IL-2 present in the composition is between 0.05 and 5.0 mg/ml (column 6, lines 47-50). Furthermore, the composition contains between 2 and 6 w/v % sucrose (column 2, lines 47-48). In addition, the reference teaches a stable pharmaceutical composition maintained at a pH between 5 and 8.5 (column 5, lines 31-34). Hora et al. also teaches the reconstitution of the lyophilized protein in water (page 8, lines 30-34).

It would have been obvious to one having ordinary skill in the art at the time the instant invention was made to modify the IL-2 containing histidine composition, disclosed in Patel et al. with the appropriate concentration of IL-2, the addition of sucrose and maintaining it at a pH between 5 and 8.5 as disclosed in Hora et al. Since Hora et al. teaches that the addition of amino acids, sucrose and salt stabilizes IL-2 proteins and maintains it soluble (abstract). Thus the claimed invention would have been *prima facie*

obvious as a whole at the time the invention was made, especially in the absence of evidence to the contrary. Therefore, claims 1-3, 5 and 9 are obvious over Patel et al. (U.S. Patent No: 5,358, 708) in view of Hora et al. (U.S. Patent No. 5,078,997).

5. Claims 1-6 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Patel et al. (U.S. Patent No: 5,358, 708) and Hora et al. (U.S. Patent No. 5,078,997) in view of Yasushi et al. (U.S. Patent No: 4,645,830).

The instant invention is directed a pharmaceutical composition comprising human IL-2 or a variant stabilized with amino acids, sucrose and salt.

The relevance of Patel et al. and Hora et al. has been set forth above in paragraph 3 and 4. However, Patel et al. and Hora et al. do not explicitly recite a pharmaceutical composition comprising human IL-2 or a variant stabilized with amino glycine and NaCl. Yasushi et al. discloses stable IL-2 compositions that contain glycine at a concentration of 5-50mg/ml (column 2, lines 50-63).

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time invention was made to add glycine also has a stabilizing agents to the IL-2 disclosed in Patel et al. and Hora et al. to produce stabilized IL-2, with a reasonable expectation of success, because Yasushi et al. teach that the loss of activity due to lyophilizing is minimized in stabilized IL-2. Therefore, the claims are obvious over Patel et al. (U.S. Patent No: 5,358, 708) and Hora et al. (U.S. Patent No. 5,078,997) in view of Yasushi et al. (U.S. Patent No: 4,645,830).

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6. Claims 1-6, 9 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Patel et al. (U.S. Patent No: 5,358, 708) and Hora et al. (U.S. Patent No. 5,078,997) in view of Yasushi et al. (U.S. Patent No: 4,645,830) and further in view of Shanafelt et al. (WO 996018A1).

The instant invention is directed a pharmaceutical composition comprising human IL-2 or a variant stabilized with amino acids, sucrose and salt.

The relevance of Patel et al., Hora et al. and Yasushi et al. has been set forth above (see paragraphs 3, 4 and 5). However, the above references do not explicitly recite the use of IL-2 variant (N88R) in a pharmaceutical composition. Shanafelt et al. discloses both the IL-2 and the N88R variant of IL-2 in pharmaceutical compositions for therapeutic uses (page 6, lines 25-30). Therefore, it would have been obvious to one of ordinary skill in the art, at the time the invention was made to stabilize the interferons disclosed in Shanafelt et al., utilizing amino acids, sucrose and salt described in Patel et al., Hora et al. and Yasushi et al. to produce stabilized interferons for pharmaceutical formulation, because the references teach that the stabilized interferons can be lyophilized and then reconstituted with little loss in activity. Thus the claimed invention would have been *prima facie* obvious as a whole at the time the invention was made, especially in the absence of evidence to the contrary. Therefore, the instant invention is obvious over Patel et al. (U.S. Patent No: 5,358, 708) and Hora et al. (U.S. Patent No. 5,078,997) in view of Yasushi et al. (U.S. Patent No: 4,645,830) and further in view of Shanafelt et al. (WO 996018A1).

7. No Claims are allowable over prior art.

### Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon whose telephone number is 703-305-1112. The examiner can normally be reached on M-F: 8:30-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 703-308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-0294 for regular communications and 703-308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

JS  
July 29, 2002

*Gary L. Kunz*  
**GARY L. KUNZ**  
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